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Bronchial leiomyoma in a chemical warfare victim—a causative agent or an incidental finding: A case report

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ABSTRACT

INTRODUCTION: Bronchial leiomyoma is one of the rarest benign tumors of the lower respiratory system, compromising less than 2% of reported benign pulmonary tumors. Chemical warfare is a known cause of chronic pulmonary diseases in soldiers who survives of the chemical wars. Most of these patients are chronically under treatment by respiratory drugs and acute exacerbations of their symptoms prompt for investigations for diagnosis of a new complication in these patients.
PRESENTATION OF CASE: In this case report we present a 43 y/o male chemical warfare victim who was under treatment for his respiratory disease for near 20 years but at last bronchial leiomyoma was diagnosed as the cause of exacerbation of his symptoms. He was undergone right thoracotomy and sleeve resection of left main bronchus. Severe adhesions plus lymphadenitis in the mediastinum might be due to the effects of prior inflammatory process.
DISCUSSION: Because of rarity of this tumor, bronchial leiomyoma in this patient may be the result of previous exposure to nitrogen mustard but the exact relationship remained to be confirmed.
CONCLUSION: Although the association between chemical warfare and lung neoplasias has not been well understood, it is the first time that a bronchial leiomyoma is reported in a nitrogen mustard survivor.

1. Introduction

Bronchial tumors are often overlooked as the cause of mild respiratory symptoms until they reach an advanced stage, especially in patients with long-term asthma or other chronic obstructive pulmonary diseases. Most of these tumors are malignant (mostly squamous cell carcinoma and adenoid cystic carcinoma) and benign tumors only account for 5–10% of the resected cases.[1] The origin of these tumors may be mesenchymal, epithelial or any of the submucosal cells. Among these, bronchial leiomyoma which is thought to arise from smooth muscles of the submucosa is the rarest type and only accounts for 2% of these neoplasms.[2] Because of the rarity of these tumors their epidemiology is not fully understood but in most reports they are most common before the fourth decade of life with a male preponderance in children.[3] Many treatment options are available for theses tumors according to their location, size and presentation such as laser or argon beam ablation, sleeve resection, pulmonary lobectomy or pneumonectomy. In this case report we present a 43 y/o male victim of Iran–Iraq war who was finally diagnosed to have an endobronchial leiomyoma as the cause of acute exacerbation of his chronic symptoms.

2. Case report

In autumn 2011, a 43 y/o male was referred to thoracic surgery ward of Imam Reza Hospital, Tabriz University of medical sciences, Tabriz, Iran. He was chronically under treatment by bronchodilators because of his chronic obstructive respiratory symptoms and exertion dyspnea which were documented that were due to exposure to chemical weapons (Sulfur mustard) during the Iran–Iraq war in 1986. After his initial 6 months treatment for skin and respiratory complications of his injuries, during this 23 years period he received several short courses of systemic and/or oral antibiotics in combination with corticosteroids and bronchodilators mostly local salbutamol and ipratropium hydrobromide sprays. He also was undergone several times of bronchoscopy which revealed diffuse inflammatory changes without any major stenosis in the large airways. His skin disease only included skin dryness, hyperpigmentation and minor signs of contact dermatitis which treated periodically only by local emollients. His respiratory symptoms were exacerbated periodically due to upper respiratory bacterial or viral infections during this period especially in falls and winters, but his disease symptoms were stable without any need for hospital admission during the last 10 years. His smoking history included

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Fig. 1. Preoperative chest X-ray.

at least 10 cigarettes/day for more than 20 years but his abstinence history was at least 6 months.

One month before admission his symptoms exacerbated again and his physician treated him by oral azithromycin and acetaminophen plus bromhexine as a mucolytic. He had no hemoptysis and his cough was not productive. Because of high fever (39.2 °C) a chest X-ray obtained which revealed diffuse haziness in both lung fields which was not different from his previous graphies except for focal infiltration in left inferior lobe plus mild bronchial deviation and elevation of the left diaphragm (Fig. 1). Skin PPD test was negative and sputum culture and microscopic smear was positive for Gram positive cocci. Systemic ceftriaxone was started with a diagnosis of pneumonia and at the same time a chest computed tomography (CT) scan was obtained. A distinct mass was revealed in the left main stem bronchus plus lingular lobe atelectasis and hyperinflation of the other lung field especially in the right side (Figs. 2 and 3). Many calcified lymph nodes were seen in both hilar areas which were attributed to his previous inflammatory conditions due to chronic sequels of chemical warfare injuries. He was admitted in hospital and a flexible bronchoscopy was done for obtaining tissue diagnosis. His condition was better as this time but the cough and chest pain still remained. A soft tissue mass with

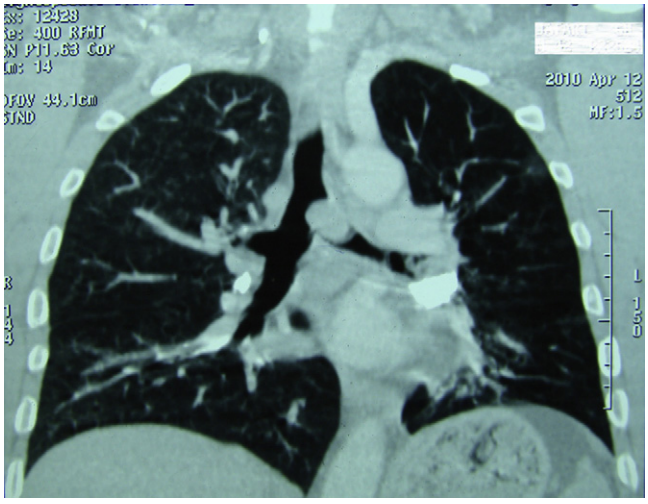

Fig. 2. Preoperative CT scan (coronal section).

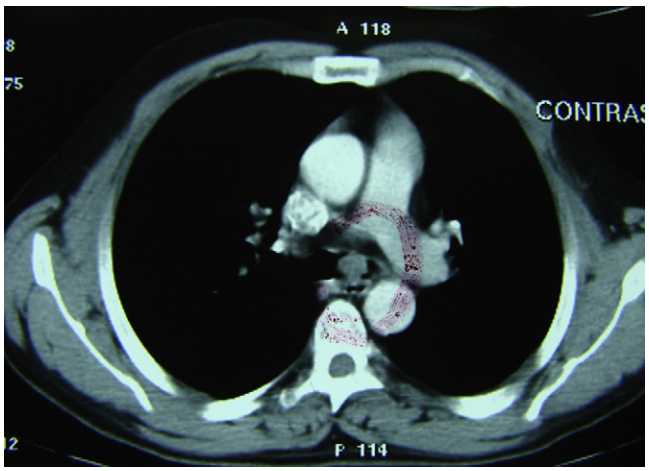

Fig. 3. Preoperative chest CT scan (transverse section).

smooth border was seen plus thick secretions which culture is positive for streptococcus pneumonia. Biopsy was done which was not diagnostic because the specimen only contained respiratory mucosa with signs of chronic inflammation.

A rigid bronchoscopy performed for better evaluation of the anatomic location of the tumor and obtaining a larger tissue fragment for pathologic evaluation. The site of the tumor was 10 mm distal to the carina and the main bronchus was normal distal the tumor with normal margins of the lobar bronchi. Pathologic sections showed fragments of chronically inflamed respiratory mucosal tissue plus proliferation of spindle cells in whorl pattern in the submucosal area. No atypia, mitosis or necrosis was seen (Fig. 4). Immunohistochemical staining for S100, desmin and actin confirmed that the spindle cell part of this tumor was actually a leiomyoma (Fig. 5).

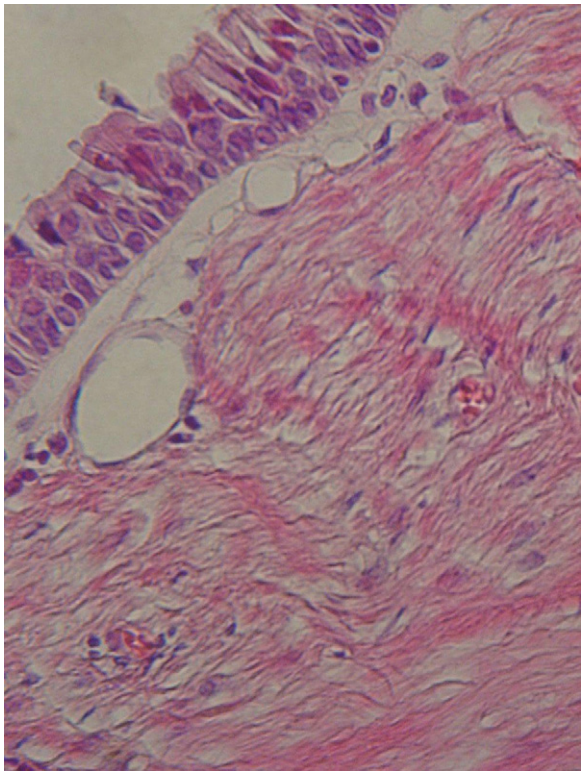

Fig. 4. H&E staining of the specimen.

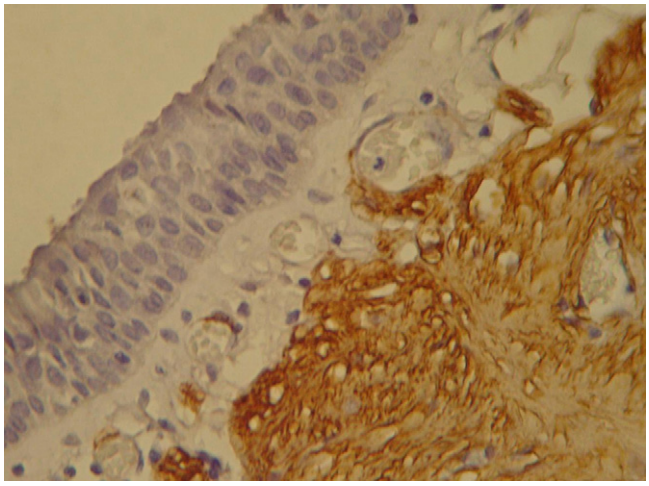

Fig. 5. IHC actin staining of the specimen.

Fig. 6. Chest CT Scan 8 months after the surgery.

He underwent a right lateral thoracotomy and a local sleeve resection of the left main bronchus with primary end to end anastomosis was done in standard manner. Safe cut margin of the distal left main bronchus during surgery was confirmed by frozen section pathologic evaluation. Severe adhesions with lymphadenopathy were found in the mediastinum due to previous inflammatory processes. Several lymph nodes were resected for pathologic evaluation which revealed only nonspecific chronic inflammatory changes. He discharged after 10 days in good condition and postoperative course was without any complication. Postoperative CT scan 8 month after the operation is shown in Fig. 6.

3. Discussion

Literature is full of case reports about many different types of tracheobronchial tumors, but benign and malignant primary bronchial neoplasm are overly rare compared with much more common tumors of the larynx and lungs. Most primary bronchial neoplasms are malignant in nature and squamous cell carcinoma and adenoid cystic carcinoma account for more than 80% of these cases.[4] The most common type of benign bronchial tumors is benign pleomorphic adenoma and bronchial leiomyoma is the rarest of these tumors that accounting only for 1–1.5% of all lung tumors with updated total number of 80 cases in the world literature.[5] Lung leiomyomas may be intraparenchymal, endotreacheal or endobronchial locations (approximately 33% of all pulmonary leiomyomas).[6]

Because of their location, patients with these types of tumors often presents with respiratory symptoms that mimic signs and symptoms of asthma, but if they grow enough the obstructive condition may results in atelectasis and pulmonary infection as in our case. Some cases may be associated with chronic cough and hemoptysis that prompt the physician for obtaining a chest X-ray or performing a flexible or rigid bronchoscopy. Specimen which is obtained by flexible bronchoscopy usually is not enough for definite diagnosis. Rigid bronchoscopy will be greatly helpful for locating the exact site of the tumor and obtaining a larger specimen. We should have a definite histologic diagnosis for planning a limited resection rather than a more radical resection of the lung. These lesions may be difficult to differentiate from fibromas, neurofibromas, or neurilemomas with ordinary hematoxylin and eosin stains and Immunohistochemical assays are necessary for confirming the diagnosis especially when we want to perform a limited resection or use minimally invasive techniques such as laser ablation or electrocauterization for their treatment.

Smoking, asbestos, chromium, arsenic, cadmium, silica, nickel, welding fumes, diesel exhausts, polycyclic aromatic hydrocarbons (PAHs), and ionizing radiation exposure by radon are among the known risk factor for squamous cell carcinoma of the tracheobronchial tree but there is no confirmed association between these risk factors and other type of bronchial tumors including leiomyoma.[7] Also, association between chemical warfare and lung cancer was not well understood but many reports in the literature have confirmed that sulfur mustard may decreased the age at which people were at risk of developing lung cancer and also increase the rate of lung cancer in the victims.[8–11]

In the acute phase, sulfur mustard which is an alkylating agent, may be rapidly results in bronchiolitis obliterans or "mustard lung" but the chronic effects of this type of chemical warfare poisoning in the victims remained to be depicted.[11] Only a few seconds of exposure to this relatively odorless gas is enough for developing the symptoms. Tissue damage will be microscopically evident after 16 h. Full body blistering and degloving and severe respiratory symptoms due to alveolar damage will be a devastating complication in non-decontaminated soldiers.[12] If left untreated most of the victims will die due to multiorgan failure. Chronic respiratory symptoms such as asthma, bronchiectasis, bronchitis, bronchiolitis, sinusitis, and bronchial stenosis are among the common symptoms in the survivors.[10] Chronic complications are due to the adverse effect of this agent on immunoregulatory pathways and also mutations in important oncogenes or tumor suppressor genes such as p53 or KRAS with a known increase in lung cancer risk.[13,14] Unfortunately, long term epidemiological studies are required for confirming the association of this type of poisoning with lung cancer. Now near 8500 Iranian veterans with well-documented exposures to mustard gas are under investigation for confirming the long term carcinogenicity of this agent.[10] Lung, nasopharynx, thyroid gastrointestinal and skin cancers and also different types of leukemia are among the malignancies which were reported in these cohort but urogenital cancers was not increased in these patients.[10] Deaths from respiratory cancer occurred in 2.5% of those American veterans who exposed to sulfur mustard in World War I. In the study of Japanese factory workers, respiratory tract tumors accounted for 58% of all reported malignant tumors (16% of all deaths).[13] One study reported 8% squamous metaplasia in those who were evaluated for diagnosing the cause of hemoptysis.[15] Some studies reported increase in the rate of benign tumors in animal studies such as benign neoplasms of the forestomach (squamous papilloma) but researches in this field are rare and inconclusive.[13] We do not find any reported association between this type of injury and benign tumors such as bronchial leiomyoma in the literature and this may be the first time that such lesion is reported in a sulfur mustard victim. Future studies are needed to better evaluate the effect of this agent on developing benign neoplasias in human.

Conflict of interest statement

None.

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Ethical approval

Obtained.

Author contributions

All authors contributed.

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